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PARAQUAT

AN OVERVIEW

PREPARED FOR

THE MINISTRY OF THE ENVIRONMENT

BY

THE PESTICIDES ADVISORY COMMITTEE

January, 1983

SB
952
.P28
O57
1983
MOE

Ministry
of the
Environment
Ontario

The Honourable
Keith C. Norton, Q.C.,
Minister

Gérard J. M. Raymond
Deputy Minister

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PARAQUAT - AN OVERVIEW

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GRAMOXONE (paraquat 200 g/L) is a restricted herbicide in Ontario, and is classified as a Schedule 2 pesticide under the Pesticides Act.

PARAQUAT

AN OVERVIEW

SUMMARY

Current information from scientific studies shows that there is no high risk in using paraquat if it is used at the recommended dilution of 0.5%, and appropriate protective clothing is worn. On the other hand, concentrated paraquat, which is the material usually involved in accidents and intentional poisonings, is very toxic and caustic to the skin, eyes and fingernails. It must, therefore, be handled with great care to minimize exposure. It is very important that persons handling both the concentrate and dilute materials follow the safety precautions on product labels.

The skin affords some protection against dilute paraquat but absorption may take place through cuts and abrasions. At the 0.5% concentration, an applicator would have to absorb or drink about 0.5 litres (1 pint) to reach a toxic dose.

In cases of fatal poisoning, the kidneys and liver are damaged to some extent, but the most severe effect is found in extensive fibrosis of the lungs which preferentially absorb paraquat from the blood. The chances of taking spray droplets into the lungs are slight, since most sprayers produce droplets in the range of 50 to 200 micron diameter, which are 5 to 20 times larger than those reaching the lung through inhalation. Larger droplets trapped in the nose can cause

nasal irritation. Moreover, it has been shown that in field practice, the concentration of airborne paraquat is only 1% of the T.L.V.

Since paraquat has a very low volatility, vapour is not a problem. On exposed moist surfaces, and in water, it is broken down under the influence of sunlight. However, it is often very persistant in the soil or in water, where it quickly becomes tightly bound to particles of clay or organic matter, where it remains immobilized and biologically inactive. There is evidence that some animals have experienced lesions on the mucous tissues of the mouth and nose as a result of feeding on freshly sprayed foliage. It has been reported that when animals were fed treated plants continuously over a long period of time, a non-fatal poisoning occurred. The animals recovered completely upon removal of the treated forage from the diet. There is no evidence of bioaccumulation in the food chain. The breakdown products of paraquat are much less toxic than the original material.

There is no known antidote for paraquat, but prompt medical attention will reduce risk of a fatal outcome.

ONTARIO PESTICIDES ADVISORY COMMITTEE

OVERVIEW -- PARAQUAT

Paraquat (Gramoxone) is a heterocyclic cationic compound that is referred to as a bipyridylium or quaternary ammonium compound. The dichloride salt is freely soluble in water, and is stable except under alkaline conditions. It is used widely as a nonselective herbicide on crop and noncrop land, and is applied as a directed spray for weed control in orchards, nurseries, and in landscape preparations. It has also been used in combination with a selective residual type herbicide for "zero-tillage" in corn production. It is sold as a 200 g/1 formulation. There is also a soluble granular formulation containing 2.5% paraquat.

Concern about the safety of paraquat was raised because of a recent poisoning case which was transferred to the Toronto General Hospital. There were conflicting reports concerning the circumstances of the poisoning. During its history, there have been many cases worldwide of paraquat poisoning, mostly resulting from deliberate ingestion of the product. Pathological changes have been noted at autopsy in fatal cases, indicating mainly lung, liver and kidney damage. The most striking change noted is widespread pulmonary fibrosis.

It is very difficult to classify paraquat on the basis of the acute oral LD_{50}, as such studies only take into account one aspect of toxicity.

The main danger of paraquat poisoning is from ingestion, deliberate or accidental, of the concentrated solution. Symptoms following ingestion consist of a burning sensation in the mouth, abdominal pains, nausea, vomiting, and diarrhea which occasionally may be bloody. It should be noted that the absence of gastrointestinal symptoms does not preclude diagnosis of oral ingestion. These symptoms are related to the concentration of paraquat swallowed and the presence of an emetic found in the concentrate. This emetic is purposely added to the concentrate which is marketed in Canada under the trade name Gramoxone. Two to three days after ingestion there may be reversible renal and/or liver damage. Five to twelve days after ingestion there may be an onset of pulmonary problems resulting in pulmonary fibrosis, finally resulting in death from respiratory failure. If pulmonary symptoms have not developed within fourteen days, they will not develop. In some cases, the dose ingested is so large that acute shock and death from multi-organ failure results.

ENVIRONMENTAL IMPACT

1. Natural Environment

(i) Paraquat is immediately inactivated upon contact with the soil, as it is almost irreversibly bound to clay mineral particles. There is, in addition, binding to organic matter. There is indication that microbial degradation and/or photolysis plays a minor role in the degradation of paraquat in the soil. In soils of low clay mineral content there is a greater possibility of leaching down to deeper depths once the binding sites have been saturated in the soil. In general, however, the paraquat cations are held so tightly that residues are not biologically available, and therefore, rendered inactive. Paraquat is not transported in the vapour phase. It can only be removed from adsorbents by boiling the clay or organic matter with strong sulfuric acid.

Normal rates of paraquat causes a slight increase in the activity of ammonifying bacteria, and in the activity of aerobic nitrogen-fixing bacteria in slightly acidic calcareous soil. The activity of the denitrifying micro-organisms decreases slightly. One field experiment reported the annual rate of paraquat loss from soil to be approximately 10%, with an half-life of approximately 6.6 years. It was concluded that paraquat present in quantities below the strong absorption capacity of the soil is either progressively bound by a mechanism that survives the analytical procedure which involves digestion of the soil with sulfuric acid, or it is degraded. (Hance, et al., 1980).

(ii) Paraquat is extremely toxic to plants, and death to plant cells is so rapid that little translocation of paraquat takes place. The cations from paraquat are reduced to free radicals in plants by electrons generated from photosynthesis, and these free radicals, in turn, react with water and oxygen to form hydrogen peroxide which kills the cells. Under conditions of reduced photosynthesis there is a reduction in the speed of killing, and this leads to a greater translocation of paraquat. There is no apparent degradation of paraquat in the plant tissue. Under strong sunlight, paraquat is broken down on the surface of living and dead plants, and may be completely degraded in two to three weeks.

(iii) There is no evidence for a build-up (bio accumulation) in plants or animals of paraquat. There is evidence, however, that there may be a build-up in soils following years of application, but this is biologically inactive.

iv) In water, paraquat is removed by organic matter, aquatic vegetation, or by suspended soil particles. It is broken down by photolysis if the water is exposed to strong sunlight and some minor breakdown results from microbial action. Photo-chemical decomposition in intense light may result in a 25% to 50% breakdown in three weeks in the absence of other factors normally present which will enhance its removal.

(v) Paraquat has no known insecticidal activity and is safe to aquatic insects when used at rates recommended for aquatic weed control.

(vi) Research work indicates that fish are not injured when paraquat is used for aquatic weed control at recommended dosages. Paraquat poisoning may become apparent if excessive rates are used. On other species of marine animals, paraquat had varying effects. Bony fish died after one-hour exposures to 10 ppm of paraquat in the water. At this concentration, snails died 24 hours after exposure, and crustaceans 36 hours after exposure. As these levels of paraquat are rarely, if ever, met in the environment, it was concluded that the toxicity of paraquat be regarded as moderate. It was also reported, but not confirmed, that the respiratory system was the system most affected by paraquat. It was also found that crayfish, both adults and juveniles, when exposed to paraquat in water, used significantly more oxygen, and that the death rate increased with length of exposure.

(vii) No bird or mouse kills have been reported from areas where paraquat has been used to control grass and weeds beneath orchard trees. There has been some indication that cattle and sheep eating sprayed vegetation have consumed enough paraquat to cause non-fatal illness. There may be some effect on birds if sprayed in the open if spraying is done by aircraft. Hares may also be adversely affected after contacting freshly sprayed (wet) vegetation.

(viii) There have been a number of deaths of dogs due to paraquat, but the circumstances concerning the exposure have not been identified. Recent data indicate that dogs may be adversely affected if sprayed grass is consumed.

(ix) Paraquat has no olfactory or gustatory repellency to bees. It has little impact on the bee when recommended rates are followed. Its use can, however, reduce the foraging areas for bees, and thus reduce the yield of honey.

(x) Paraquat is registered in Canada for many uses, some of which are:

a) Suppression of grasses and annual weeds in established legume crops.

b) Pasture renovation.

c) Control of weeds in corn where ZERO-TILLAGE is being practiced.

d) Weed and grass control beneath fruit trees and berry bushes.

e) Weed and grass control in asparagus and other vegetable crops.

f) Weed and grass control in potatoes.

g) Weed control in nursery crops.

h) Turf renovation and weed control in flower beds, etc.

i) Non-crop lands including limited aquatic areas.

2. Environmental Health - Toxicology of Paraquat

(i) Acute Toxicology

Acute Oral LD_{50}

104 mg paraquat ion/kg	-	mouse
120 mg paraquat ion/kg	-	rat
693 mg formulation/kg	-	rat
30 mg paraquat ion/kg	-	guinea pig
362 mg paraquat ion/kg	-	hen
35 mg paraquat ion/kg	-	cat
70 mg paraquat ion/kg	-	sheep
75 mg paraquat ion/kg	-	monkey
126 mg paraquat ion/kg	-	rabbit
25-50 mg paraquat ion/kg	-	dog
35 mg paraquat ion/kg	-	hare
50 mg paraquat ion/kg	-	cow

Acute Dermal Toxicity LD_{50}

236 mg/kg	paraquat ion	-	rabbit
480 mg/kg	paraquat dichloride	-	rabbit

Sub-Acute Dermal Toxicity

4.5 mg/kg for 20 days	-	rabbit: Causes some irreversible proliferation of lungs.

Acute Inhalation

Paraquat is non-volatile and thus creates no fumes.

LC_{50} - 0.5 ug/l for rats (2-3 u size droplets)
NOEL - 0.01 ug/l for rats (2-3 u size droplets)
Droplets in excess of 10 u not respirable (Gregoria, 1982)

Acute Human Toxicity LD_{50}

40 mg/kg of paraquat ion - man*

(2 - 4 g of paraquat ion fatal to man.*)
(14.2 - 28.3 g. product fatal to man.*)

---

* Determined from cases involved in paraquat poisoning.

Feeding Studies

Fish

In bluegills the 24 hour LC_{50} for paraquat ion was found to be 500 ppm and for harlequin fish it was reported to be 840 ppm. The surfactant usually causes fish mortality before the paraquat ion.

Chickens

A test using domestic fowl suggests that the intravenous administration of paraquat may give rise to increases in renal peritubular blood flow. The amount of paraquat administered was 25 mg/kg.

Paraquat ingested by poultry was deleterious to the viability of eggs, the hatching rate, and the chick development.

Rats

60% mortality resulted when rats were fed 50 mg/kg/day for five days.

Dogs

Dogs fed 85 and 170 ppm of paraquat in daily diet for 27 months showed lung and liver abnormalities.

Cattle and Sheep

Some deaths were reported in a test utilizing cattle and sheep that received 25 mg/kg/day for six or seven days.

Monkeys

Cynomologus monkeys were used in a study to determine toxicity and renal functioning following the administration of paraquat. A single injection of 6 mg/kg paraquat was not lethal to the monkeys, but all higher dosages were. The 45 mg/kg oral dose did not prove fatal, but all higher dosages did. Clinical signs consisted of vomiting, anorexia and dyspnea. There was acute renal (kidney) failure, accompanied by oliguria (small amounts of urine), high plasma urea and metabolic acidosis. Pulmonary damage followed renal failure and was the cause of death. Animals surviving the acute phase of toxicity had interstitial pulmonary fibrosis.

No Effect Levels

Rats

Rats that have been fed paraquat for 24 months at the rate of 170 ppm of paraquat ion in their daily diet showed no adverse effects.

When fed 25 mg/kg/day for a period of ten days, no ill effects were found upon examination.

Cattle and Sheep

Cattle and sheep fed 5 mg/kg/day for a period of ten days showed no ill effects.

Dogs

Dogs fed 0.5 mg/kg/day of paraquat in their diet for ten days showed no ill effects.

General

Eyes

Paraquat, if applied to the eyes of the rabbit at the rate of 0.2 ml of a 50% solution will result in a mucopurulent discharge (yellow discharge) with corneal opacification (cataract), accompanied by severe iritis (inflamation of the iris), and conjunctivitis (pink eye), and finally death.

(ii) Mutagenicity

Paraquat has been shown to possess mutagenic properties *in vitro* using microbial test systems. *In vivo* testing, using mice as the test animal, indicate that in mice, no mutagenicity occurs (Selypes, *et al.* 1978).

Paraquat was positive in the *in vitro* repair tests and the 8-azaguanine resistance system when Salmonella typhimurium was the test organism. When Aspergillus nidulans was used, it was also positive for gene mutations and lethal recessive damage inductions.

There is evidence that would indicate that DNA should be considered as a possible macromolecular target for the lethal effects of paraquat.

Paraquat has been reported to inhibit DNA synthesis both *in vivo* and *in vitro*. Further testing following these findings indicates that the molecular mechanism of inhibition of cell growth and DNA synthesis may be due to the inhibition of DNA polymerase by paraquat.

As both positive and negative mutagenic responses have been reported, a definite conclusion is impossible at this time.

(iii) Teratogenicity

In a review carried out in 1972, Durham and Williams reported that in studies utilizing experimental animals, some evidence of possible teratogenic results were found when paraquat was tested. No evidence indicating human teratogenicity was reported. (Gregorio, (1982); Khera, et al. (1970); Bus, et al. (1975), and Hodge, et al. 1978)).

(iv) Tumorigenesis

Paraquat was administered intraperitoneally in low doses to CFLP female mice. This treatment resulted mainly in toxic damage to the alveolar epithelium. However, paraquat did significantly enhance the number of lung tumors induced by urethan two days after the paraquat exposure occurred. This was a dose dependent effect. The paraquat may have enhanced the carcinogenicity of urethan by increasing the number of proliferating target cells in the lung. (Bojan, et al. 1978).

PARAQUAT POISONING IN HUMANS

(i) Ingestion

While fatal poisonings with paraquat have occurred, most of these fatal cases have resulted from deliberate ingestion.

Autopsies reveal that in fatal cases there is evidence of mainly lung, liver, and kidney damage. Some cases have had signs of multi-organ damage including myocarditis, adrenal necrosis and cerebral damage. The most striking change in the fatal cases has been the widespread pulmonary fibrosis in the lungs. This has also been found in fatal cases where the route of absorption has been other than oral. Pharmacokinetic studies in dogs and humans indicate that paraquat in low concentrations in the systemic circulation is rapidly cleared by the kidneys. When the system becomes overloaded, however, the kidneys are permanently damaged and paraquat is stored in body muscle. It is felt by many medical research people that the presence of more than 0.2 ug/ml of paraquat in the plasma, at 24 hours after the time of ingestion may be fatal. Ten to fifteen milliliters of formulated product (20% active ingredient) are considered as a potentially lethal oral dose for adults. Ingestion of over 50 ml of the 20% product is almost always fatal.

Symptoms

Immediate

Symptoms following ingestion consist of a burning sensation in the mouth, abdominal pains, nausea, vomiting and diarrhea which occasionally may be bloody. In some cases, the dose ingested is so large that acute shock and death from multi-organ failure results.

It should be noted that the absence of gastro-intestinal symptoms does not preclude diagnosis of oral ingestion. These symptoms are related to the concentration of paraquat swallowed and the presence of an emetic found in the concentrate.

2 - 3 Days Later

Two to three days after ingestion there may be reversible renal and liver damage.

5 - 12 Days Later

Five to twelve days after ingestion there may be an onset of pulmonary problems resulting in pulmonary fibrosis, finally resulting in death from respiratory failure.

14 Days Later

If pulmonary symptoms have not developed within two weeks following ingestion, they will not develop.

(ii) Skin Absorption

There have been some cases of systemic poisoning resulting from skin absorption of paraquat, but these, in general, have been due to prolonged contact with concentrated solutions. Inhalation of paraquat from using conventional type spraying equipment is not normally expected, since the spray is generally directed downward and the droplet sizes are too large to penetrate beyond the upper respiratory tract.

It has been reported by Staiff, et al., 1975, that the results of their studies on dermal and respiratory exposure to paraquat indicates that the hazard to both field applicators and persons using yard and garden pressurized dispensers should be minimal if safety measures are followed. While skin offers a good protection against paraquat penetration, any cuts or abrasion of the skin increases the possibility of absorption. Paraquat is caustic to skin and eyes, and special attention should be placed in preventing splashes from contacting the skin, entering the eyes or the mouth. If such does occur, wash immediately with water and call a physician.

In Malaysia, workers have been spraying 0.5% to 0.1% paraquat solutions since the early 1960s. While a few have reported local skin and mucous membrane effects, no systemic complications have resulted through skin absorption. Local effects can occur if spillage takes place as well as from prolonged exposure. These are easily taken care of by prompt treatment. One fatality occurred through percutaneous absorption when the spray operator applied a 5% solution. Some have died by applying the concentrate to the body to kill body lice.

It has been reported that in animal tests, dermal toxicity has not occurred when up to 1 lb. paraquat ion in 10 gallons of water was tested. A dermatitis could be encountered if contaminated clothing from a 1% spray were to be worn for an extended period of time.

(iii) Other Reported Dermal Effects

A summary of dermal effects has been recorded from surveys of manufacturing and formulating plants, and the following have been recorded:

a) Any cuts or abrasions of the skin are slower in healing if they become contaminated with paraquat.

b) The spilling of concentrate on the skin, if not washed off immediately, will cause irritation, and dermatitis may result.

c) The concentrate could, upon contact with the fingernails, cause loss of fingernails if not washed immediately after exposure. Damage or loss of nails is not permanent.

d) A splash of concentrate into the eye can cause severe eye irritation. However, if splashes are treated promptly by thorough irrigation with water and further medical treatment, no serious injury should result.

e) It was reported by Dr. A.A.B. Swan, 1969, that a medically supervised survey of spray applicators in Malaya applying a dilute aqueous solution of paraquat was carried out. The six men in the study sprayed all day, six days a week, for a period of 12 weeks, using knapsack sprayers. Each man sprayed an average of 2,600 gallons of spray solution. Two cases of local effects were cited in the report.

f) In a clinical study of non-fatal accidents involving paraquat and agricultural workers from 1967 to 1976, some 67 cases were reported during actual application. In addition, four cases of splashing of concentrate into the eyes, seven cases of dermatological burns, and four cases of oral lesions were caused by either sucking or blowing on the spraying apparatus or hand to mouth contact. Factors contributing to poisonings included spraying into the wind, leaky spraying equipment, splashing of concentrate before dilution, inadequate dilution of the concentrate, carelessness in personal hygiene, incorrect apparatus, and spraying within a confined indoor space without proper protective equipment. Widespread disregard of basic safety precautions among sprayers was noted. (Cravey, 1979).

g) A study to consider the health of workers was carried out in 1982 by Chester and Woolen on the occupational exposure to paraquat by plantation workers in Malaysia comprised of quantative estimates of dermal and respiratory exposure of knapsack operators, carriers, and rubber tappers, operating under their normal working conditions. Spray operators are dermally exposed as they walk through recently sprayed vegetation and into their own spray, by regularly adjusting and unblocking spray nozzles, and through leakage. In some cases, overfilling of the knapsack spray tanks causes further contamination of skin. Carriers are dermally exposed when they walk through the recently sprayed vegetation. Determination of the total air-borne paraquat concentrations in the breathing zone showed that spray applicators were exposed to an order of 1% or less of the current TLV for respirable paraquat. No paraquat was detected in the breathing zones of tappers working in simultaneously sprayed blocks. The authors concluded that the calculated ranges of dermal and respiratory exposure, when compared with published data on both the exposure to, and the toxicity of paraquat, indicated there should be no toxicological risk to any of the three groups studied.

h) Howard, _et al._, (1981) conducted tests on 27 paraquat spraymen (mean spraying time of 5.3 years). Tests included:

1. Pulmonary function
    - a) forced vital capacity
    - b) forced expiratory volume in lungs

c) percentage forced expiratory volume in lungs

d) single breath codiffusion

2. Renal function

   a) serum creatinine

   b) blood urea nitrogen

3. Liver function

   a) alinine aminotransferase

   b) aspartate aminotransferase

   c) alkaline phosphatase

4. Full hematological screen

No evidence was found of adverse health effects due to the spraying of paraquat.

i) General

Two groups of paraquat formulation workers in the United Kingdom were studied for possible harm due to exposure to the paraquat. The first group was involved with solid formulations, with the second group being involved with liquid formulations. Rashes of the skin, damage to fingernails, and epistasis were found in most workers due to direct contact of standard mucous membranes. No long-term effects on skin, mucous membranes, or general health was noted following exposure over several years. (Howard, 1981).

In Czechoslovakia, 67% of the pesticide accidents result from the spraying of hop vineyards with paraquat, despite the fact that hops are grown on only 0.2% of the cultivated land. Practically all of the problems arise from the failure to follow necessary safety precautions, careless operators, poor personal hygiene, poor medical supervision, and lack of education. The use of safety equipment would reduce paraquat accidental poisonings to almost nil.

In Ireland and the United Kingdom, accidental poisoning by paraquat has reduced considerably as a result of widespread publicity by the news media, but suicides using paraquat have increased.

(iv) Report on Ontario Fatality

A woman who frequently worked with paraquat in orchards was admitted to hospital after minor scratches on her legs and arms developed into raised lesions exuding both clear and bloody fluid. She also had headaches, breathlessness, chest tightness, anorexia and weight loss. Biopsy from the ulcerated lesions showed necrosis of the epidermis and dermis. Pulmonary function studies showed moderate restrictive ventilatory defect. Following 14 days of topical therapy with Burrow's solution compress and petroleum gause, marked improvement was noted, and she went home. Seventeen days later, she returned to the hospital with symptoms of dyspnea, cough, fever, nausea and vomiting, and a few new lesions. She died 12 days later. Histopathological findings, together with similarities to previously described paraquat poisoning in animals pointed to paraquat poisoning. Since paraquat is not normally inhaled in toxic doses it was speculated that quite likely only small quantities, over a long period of time, were absorbed by the woman's skin, and that over a long period the amount may have accumulated to a considerable quantity. The long-term interval between exposure and death may have been due to the small doses absorbed over a long period. No protective clothing was worn. (Newhouse, _et al._, 1978).

(v) Inhalation Toxicity

As paraquat has a very low vapour pressure it is not volatile, and, therefore, a vapour hazard is unlikely to exist. Studies with the rat show that it was necessary to produce droplets of less than 3 microns in size to produce toxic effects. Droplets larger than 3 microns in size are retained in the nose and mucous membranes, and thus do not reach the lung. Most agricultural sprayers used to apply paraquat produce droplets in the 50-200 micron range. The mist blower should not be used to apply paraquat in enclosed spaces. Over exposure to spray mist or dust of paraquat can result in bleeding of the nasal passages if inhaled.

One report cites a grinding wheel operator who, for cooling purposes, utilized a used paraquat container containing small but unknown amounts of paraquat. Constant inhalation of a very fine spray of water resulted in cough, fever and malaise. Chext X-rays showed no change to previous pictures. Complete recovery followed removal of the contaminated water being used for cooling. (Anon. B.M.J. 1981).

Acute inhalation could occur from exposure to nebulised paraquat spray. No deaths have been reported through acute inhalation of spray.

It has been reported by Dr. T. B. Hart, of ICI, that pulmonary damage from inhalation of paraquat has not been reported in 20 years of worldwide usage of paraquat.

In summary, studies carried out have shown that paraquat is normally not inhaled at levels likely to cause toxic injury during normal application.

(vi) Effects on Lungs

Paraquat is highly toxic to the lung, and is actively accumulated following absorption into the body. A specific uptake mechanism exists whereby paraquat competes with endogenous diamines. Paraquat uptake is both energy and concentration dependent. The site of paraquat storage may be the type II pneumocyte, which may also be the cell type most affected by paraquat poisoning. Paraquat can produce direct damage to pulmonary cells regardless of the method by which it enters the body. The ingestion of paraquat produces a frothy exudate in the lungs and pulmonary edema. It is only slowly removed from the type II cells in the lungs.

Increased interstitial shadows and spot-like shadows appear on the X-rays. Multiple hemorrhaging and thickening of the alveolar walls of the lung also occur.

Studies carried out on adult hooded rats to determine the effects of paraquat on the lungs indicated that, when a dose of 35 mg/kg paraquat was injected, several changes in the lung tissue took place over a period of time. Examinations made 2, 4, 8, 16, 24 and 48 hours after injection showed granulocytes occurred in the interstitium and the alveolar spaces initially, followed by lymphoid elements and histiocytes after eight hours. After 24 and 48 hours the alveolar epithelium degraded.

(vii) Effects on Kidneys

Small amounts of paraquat are actively secreted by the organic cation transport system found in the kidneys. This system can rapidly eliminate the paraquat from the body. High doses of paraquat cause a great deal of kidney damage, knocking out the organic cation transport system, and thus reducing paraquat elimination. This results in prolonged high plasma levels, and increases the tendency to damage the lungs. Necrotic kidney tubule cells may also be found upon autopsy.

(viii) Skin Irritation and Sensitization

Paraquat applied to intact skin of the guinea pig had no irritating effect at concentrations up to 10%. It caused slight erythema within 24 hours after application to gently scarified skin. Marked skin irritation was seen after intracutaneous injections in a minimum concentration of 0.5%. When applied to intact skin, paraquat had no sensitizing effect. Paraquat is not a contact allergen.

(ix) Paraquat Poisoning - Signs and Treatment

Treatment is necessary in the case of accidental or deliberate ingestion of paraquat concentrate. For humans, the fatal dose is about 15 ml of 20% concentrate per individual.

The immediate effects of ingestion are vomiting and abdominal cramps and diarrhea, followed by soreness of the mouth and throat and difficulty in swallowing. Signs of kidney and liver damage may appear within the first two or three days. With very large doses, there may also be some tremors and even convulsions. Signs of pulmonary dysfunction may develop gradually after a few days (5 - 12 days usually). At the beginning, pulmonary function tests may give abnormal results in the absence of clinical signs of lung damage. Subsequently, there may be dyspnoea with pulmonary edema, worsening to marked pulmonary fibrosis and then death, due to respiratory insufficiency.

As obvious symptoms may be delayed two to three days, it is important that all cases of paraquat poisoning be referred to a hospital immediately, where the particular formulation ingested should be ascertained and the presence of the chemical in the urine be confirmed by analysis. The following treatment has been suggested by ICI Industrial Hygiene Labs.

> "If liquid concentrate has been swallowed, the patient should be made to vomit as soon as possible, if this has not already taken place. The next step is to wash out the stomach thoroughly without delay.
>
> If some hours have passed since the chemical was swallowed, the stomach wash-out should be attempted only in the hospital because of damage which may have been to the aesophagus."

Experiments have shown that it is possible to reduce the absorption of paraquat from the gut by giving a suspension of Fuller's Earth. One litre of a 15% aqueous suspension of Fuller's Earth should be given orally, preferably by gastric tube, together with a suitable purgative e.g. mannitol (200 ml of a 20% aqueous solution). This process should be repeated until the Fuller's Earth is seen in the stools, a process which should take from four to six hours from the start time.

There is no antidote for paraquat. Treatment should be directed toward increasing excretion of paraquat. Prolonged diuresis at 10 - 20 litres of urine a day may be beneficial. It should be induced either by oral or by intravenous administration of fluids, starting as soon as possible, and continuing until urine is free of paraquat. Serum electrolytes should be closely monitored. If forced diuresis is contraindicated, consideration should be given to the use of haemoperfusion through a charcoal column to assist in removing the paraquat from the blood.

Other treatment methods that have been used include steroids, immunosuppressives, D-propranolol and penicillamine. None of these treatments have been shown to be beneficial.

Plasmapheresis:

The use of gastrointestinal adsorbents and hemodialysis/perfusion in the treatment of paraquat poisoning cases is recommended by some. There is some doubt as to the benefit of plasmapheresis.

Recoveries

A 20 year old female ingested 30 mls of a 20% paraquat solution in a suicidal attempt. Prompt action followed, and a gastric lavage was carried out, followed by forced diuresis, hemodialysis, gastro-intestinal purgation, and the administration of specific adsorbents. The patient's recovery is credited to the early institution and rigid enforcement of the treatments given. The prognosis of paraquat poisoning depends on the amount ingested and on the rapid and early removal from the gut and the bloodstream. Since 1980 an emetic has been added to ICI paraquat formulations sold in Canada. It has been shown in animal studies to increase the potentially lethal dose orally by a three to five fold factor.

MARIJUANA AND PARAQUAT

Both the United States government and the Mexican government have sprayed marijuana fields in an attempt to eliminate production. Confiscated marijuana bricks in 1976 and 1977 were analyzed for paraquat. Of 54 bricks taken in 1976, residues greater than 1 ppm of paraquat were found in 7.4% of the samples. Of 46 bricks taken in 1977, there was 19.6% of the bricks positive. Despite this, no paraquat induced lung damage has been reported in human lungs from smoking marijuana. It has been estimated that 96% of the paraquat, upon burning the marijuana, is converted to dipyridine, a chemical considered to be relatively harmless.

REBUTTABLE PRESUMPTION AGAINST REGISTRATION (RPAR)

The U.S. Environmental Protection Agency removed paraquat from RPAR and returned it to normal registration July 1, 1982. There were some restrictions placed on the aerial application of paraquat east of the Cascade and Sierra Nevada Mountains and west of the Rocky Mountains. i.e. Nevada. This is being done because of the exposure of birds and hares which have so little cover in the desert when aerial applications are made.

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